**Institution: Liverpool School of Tropical Medicine (LSTM)**

**Unit of Assessment: UOA1**

1. **Unit context and structure, research and impact strategy**

This UOA1 submission contains 54.1 FTE compared to 31 FTE in REF2014 and includes staff from all LSTM Departments: Clinical Sciences (CS; headed by Ferreira), Tropical Disease Biology (TDB; Biagini), Vector Biology (VB; Donnelly) and International Public Health (IPH; Jaffar). The departments collaborate closely (some staff have dual department appointments) which facilitates translational research. REF2021 marks the first submission for LSTM as an independent HEI (awarded 2014) which previously submitted jointly with the University of Liverpool (UoL).

LSTM creates knowledge to control or eliminate diseases afflicting the world's poorest populations. Pivotal to LSTM's success are long-lasting equitable partnerships in Low-Middle Income Countries (LMICs) and our sustained commitment to capacity strengthening. Staff work both in Liverpool and in overseas partner organisations and all Departments collaborate with industry and other delivery partners. This close relationship with industry has recently been enhanced by a **Strength in Places award** and establishment of the *Infection Innovation Consortium* (iiCON). iiCON will develop new products that directly reduce the burden of infectious diseases in the UK and around the world. The strong functional links between staff in Liverpool, staff based in LMICs and research users allow effective translation of research from bench-to-bedside (while collaborations involving staff submitted to UOA2 move translation into implementation). The same linkages ensure that LMIC research priorities become the focus of investigation in LSTM laboratories.

**CS** works across a spectrum from laboratory science, experimental medicine, epidemiology, clinical Phases 1 to 3, post-licensure Phase-4 and Systematic Reviews. Key topics include lung health (including TB), sepsis, antibiotic resistance and malaria in pregnancy. Our new facilities (see section 3) now enable vaccine trials and human challenge studies of healthy volunteers adjacent to Good Clinical Practice (GCP) laboratories.

**TDB** has translational research at its core and has emerged from a predominantly parasitological focus to a broader pathogen and snake bite portfolio. TDB has facilities and expertise that allows investigation of many human parasites (full life cycle), viruses (including HIV, COVID-19 and Dengue) and World Health Organization (WHO) priority listed bacteria (together with 20,000+ collection of bacterial and fungal isolates from the "*Swab & Send*" initiative and a Transposon Registry). The department houses a UK Home Office accredited *Herpetarium* and experimental animal facility that contains the largest collection of venomous snakes in the UK. TBD's Therapeutic Discovery facility enables the full development life cycle from chemistry, *High Throughput Screening*, pre-clinical infection models for lead optimisation, candidate selection and clinical trial optimisation against Cat II and III pathogens. The underpinning technology platforms are industry standard and the discovery focus has expanded over the past five years and now addresses malaria, TB, lymphatic filariasis, COVID-19, priority bacteria and snake bite. As a result of this environment, a rich drug development pipeline now exists at LSTM across multiple diseases.

**VB** has a research portfolio extending through functional genomics, behaviour and ecology of disease vectors, clinical trials, implementation research and the development of intervention tools. VB's strengths in molecular entomology has identified genes and pathways specific to disease vectors that are now the targets of screens to identify control tools. VB is world leading in insecticide resistance of vectors - particularly the molecular mechanisms of resistance - and has identified many of the major genes responsible. The department maintains the largest collection of insect vectors of human disease in the UK, including the most complete range of characterized insecticide resistant strains of mosquitoes globally, and hosts a Good Laboratory Practice (GLP) accredited laboratory for screening new chemicals to target these vectors.

Studies of the interactions between vectors, their microbiome and parasites have led to new understandings about disease transmission and underpinning approaches to control vector borne diseases by disrupting their microbiomes. VB research on vector behaviour has led to the development and field trials (including cost-effectiveness) of new vector control tools including new bednet designs (see Impact Case Study (ICS) LSTM102) and 'Tiny Targets' for control of Human African Trypanosomiasis (see ICS LSTM105).

**IPH** has a substantial presence in LMICs and has close interaction with communities, patients and public health bodies (e.g. the National AIDS Control Programme and National Control Programme for Non-Communicable Diseases in Uganda and the Department of Preventive Services in Tanzania). Most IPH staff have been submitted to UOA2 but clinical trial work is presented in this UOA1 submission.

**Key initiatives and awards.**

***Clinical Sciences.***
During the submission period CS staff won grants and contracts totalling **£161million (M)**; examples include:

**The International Multidisciplinary Programme to address Lung Health in Africa (IMPALA)** is a National Institute for Health Research (NIHR) Global Health Research Unit (£7M) that promotes transdisciplinary approaches and research capacity building for Lung Health in a large collaboration in sub-Saharan Africa. IMPALA focuses on tuberculosis, determinants of lung health and approaches to diagnosis of respiratory diseases in low-income countries.

**The African Research Collaboration on Sepsis (ARCS)** is an NIHR Global Health Research Group (£2.5M) with a broad trans-disciplinary portfolio that aims to optimise quality of care for adults hospitalised with sepsis in sub-Saharan Africa. ARCS' main work focuses on partners based in Uganda, Malawi and Gabon and is complemented by additional country sites (including Sierra Leone, Nigeria, Burkina Faso, Ghana, Cameroon, Democratic Republic of Congo and Ethiopia).

**Drivers of Resistance in Uganda and Malawi (DRUM)** (£3M; an MRC strategic Global Challenges Research Fund (GCRF) award) aims to understand the community carriage of extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* in Uganda and Malawi. This requires longitudinal microbiological surveillance (including whole genome sequencing) of humans, animals and the environment, alongside characterisation of water, sanitation and hygiene (WASH) and health-seeking behaviours. DRUM will generate an agent-based model and show the critical points at which public health and policy efforts should be made.

***Tropical Disease Biology.***
During the submission period TDB staff won grants and contracts totalling **£72M**; examples include:

**Drug development for 'neglected tropical diseases' (NTDs).** The Anti-Wolbachia (AWOL) Consortium, supported by over £23M since 2006 has established a rational preclinical methodological platform to assess candidate cures for filariasis. Wolbachia is a bacterial endosymbiont of filarial worms and AWOL has developed a high throughput drug screening platform to discover novel chemicals active against Wolbachia and validated a 'pan-filarial' small animal model to test anthelmintic or anti-Wolbachia drugs. Resulting drug candidates include: **ABBV-4083**, a tylosin-derivative now selected by AbbVie, LSTM and DNDi for 'orphan drug status' and 'investigational new drug status' submissions to the US Food and Drug Administration (FDA). Clinical studies have reached Phase-II. **AWZ1066, an** azaquinazoline developed by LSTM, UoL and Eisai Inc, and funded by the Japanese Global Health Innovative Technology Fund. This has successfully completed toxicology profiling and first-in human testing will start in August 2021. In addition, the basic and applied studies with doxycycline have led to

WHO approval of this treatment for treatment of lymphatic filariasis (LF) and Onchocerciasis in patient populations.

**Drug development for malaria.** Industry-standard pathways are followed (in formal product-development-partnerships with the *Medicines for Malaria Venture* (MMV)) extending from pre-clinical discovery to clinical stages of development. One such collaboration has resulted in the synthetic tetroxane **E209** which is being assessed for onward development.

**African Snakebite Research.** Two large awards (NIHR Group award, £2.5M 2017-2021; Department for International Development (DFID), £3.1M 2018-2021) have enabled formation of the world's largest multidisciplinary research group dedicated to reducing the burden of tropical snakebite. Africa's first Snakebite Research and Intervention Centres have been formed in Kenya, Nigeria and eSwatini and this collaborative biological, clinical, health economic and epidemiological research is (see ICS LSTM103) generating new clinical tools.

**Counting Time on Neglected Tropical Diseases** (**COUNTDOWN).** COUNTDOWN is a DFID - funded programme (£11M) of implementation research focused on sustainable solutions to control and eliminate 7 Neglected Tropical Diseases (NTDs). The main pillar of integrated NTD control initiatives is delivery of *Mass Drug Administration* simultaneously to treat and control disease. COUNTDOWN brings together health care providers, policy makers, laboratory scientists, research uptake specialists, Ministries of Health and Non-Government Development Organisations and presents an opportunity to bridge the knowledge to implementation gap for shared health impact, including in fragile communities.

***Vector Biology.***
During the submission period VB staff won grants and contracts totalling **£95M**; this figure excludes awards to the *Innovative Vector Control Consortium* (IVCC). Examples include:

**Development of new vector control tools.** Studies on the biology and behaviour of tsetse flies have led to simple, low cost 'tiny targets' that are now being deployed in all major remaining foci of the disease, bringing elimination of human African trypanosomiasis as a public health problem in reach. This work has been supported by £5.9M from the Bill and Melinda Gates Foundation (BMGF). We have also translated our observations on the behaviour of malaria mosquitoes when contacting insecticide treated nets into new bednet designs (supported by funding from MRC and Wellcome Trust of approximately £3M). These are now being evaluated in trials in the Democratic Republic of Congo supported by BMGF.

**Evaluation and optimisation of vector control tools.** VB has developed insecticide resistance assays that are being used by intervention programmes in Africa for monitoring vector control programmes. With funding from the National Institutes of Health, UKRI and BMGF the Department is supporting the implementation of molecular monitoring for insecticide resistance in Africa. With BMGF support (£4.4M) VB has developed new behavioural assays that are being used to evaluate the performance of insecticide-based control tools in Africa. Assays have also been developed to provide quality assurance of insecticide-based vector control; these are widely used to affect policy change for visceral leishmaniasis control in India. VB has also led several trials of new vector control tools, including the largest evaluation of a new class of insecticide treated net, which was conducted in Uganda.

**Malaria in Insecticide-resistant Africa (MiRA)**. With funding from a Wellcome Trust Collaborative Award (£1.8M), LSTM led an interdisciplinary project to determine why malaria is persisting despite high levels of coverage with insecticide-treated nets (ITNs). The project quantified the public health impact of insecticide resistance and estimated the finances required to meet malaria control targets in high burden countries where malaria is stubbornly persistent, aligning with WHO's renewed focus on 'High Burden, High Impact' countries.

**Accelerating access.** VB houses the '*Liverpool Insecticide Testing Establishment*' (LITE) which tests resistance liabilities in new public health pesticides. VB staff bring this expertise to WHO

teams to guide policies on selection and deployment of insecticide-based control tools, and work with national regulators (through the *Innovation to Impact Programme*) to expedite country access for these tools.

***International Public Health***
Most IPH awards and initiatives are submitted to UOA2; the present submission presents major clinical trial work.

**Cryptococcal Meningitis (CM) Trials.** CM is an opportunistic fungal infection of advanced stages of HIV-infection and causes approximately 15-20% of AIDs-related deaths. IPH staff have led pivotal trials that have evaluated novel approaches for the prevention and management of CM in LMICs (see ICS lLSTM101). These have identified novel low-cost biomedical strategies that have been incorporated into WHO guidelines and have led to changes in clinical practice in Africa. IPH research has stimulated investment in a generic version of flucytosine and to increase access for LMICs. The work now continues with the AMBITION trial (€10M, European Developing Countries Clinical Trials Partnership (EDCTP); Swedish International Development Agency; DFID/MRC/Wellcome Trust) of innovative short-term treatment regimens.

**Prevention and management of HIV-infection, diabetes and hypertension**. This is funded jointly by NIHR (£6.5M), EU Horizon 2020 (£3.9M) and EDCTP (£3.6M). Large-scale randomised trials are evaluating major re-organisation of health care services in Tanzania and Uganda, in partnership with health policy makers, so that they may optimally control common high-burden chronic diseases.

**Internationally leading findings**

***Clinical Sciences***
In the field of **RESPIRATORY INFECTION**, Ferreira and Collins have shown the importance of controlled inflammatory responses and mucosa-associated invariant T cells in protection against pneumococcal colonization (Jochems et al 2019, ***J Clin Invest***) while Rylance has demonstrated interactions between live-attenuated influenza vaccine, pneumococcal challenge, adult nasal microbiota and mucosal immunity using an experimental human challenge model (de Steenhuijsen et al, 2019 ***Nature Comms***). Gordon (Director of the Malawi Liverpool Wellcome trust Clinical Research Programme (MLW)) and Meghji have shown that >40% of urban Malawian adults had abnormal lung function (mostly restrictive) in the context of widespread exposure to biomass smoke and a high prevalence of HIV (Meghji et al 2016, ***Am J Resp & Crit Care Med***). Devereux undertakes large scale NHS-based trials and cohort investigations of respiratory disease and its treatment (Devereux et al 2018, ***JAMA***). Research on **TUBERCULOSIS** in LMICs often implies its interaction with HIV and Jambo (who is based in MLW) has shown that HIV preferentially infects small alveolar macrophages resulting in selective impairment of phagocytic function (Jambo et al 2014, ***Mucosal Immunology***), while Mwandumba (Deputy Director of MLW) has investigated HIV disease in an African setting (Kelly et al 2019, ***JID***). Using spatial modeling MacPherson (also based in Malawi) has defined the main drivers of disparity in TB outcomes and addressed these in cluster randomised trials (Horton et al 2016, ***PLOS Medicine***). Caws works on multi-drug-resistant TB in South Asia and has demonstrated the transmission dynamics of Mycobacterium TB in Ho Chi Minh City (Holt et al 2018, ***Nature Genetics***). Working on **SEVERE INFECTIONS,** Jacob has developed a real-time PCR TaqMan array card for use in field settings for outbreak investigation (Liu et al 2016, ***J Clin Microbiol***). Other work in high-severity infection by Fletcher has advanced understanding of coagulopathy in Crimean-Congo haemorrhagic fever (Fletcher et al 2019, ***Lancet Infect Dis***), and Morton has demonstrated the importance of neutrophil extracellular traps (NETs) in sepsis, and potential immunomodulatory therapies in bacterial infection (Abrams et al 2019, ***Am J Resp Critical Care Med***). Iroh-Tam has studied antibiotic resistance in paediatric bloodstream infections (Iroh-Tam et al 2018 ***Clinical Infectious Diseases***). Working on **SALMONELLAE,** Feasey (based in the MLW Programme) has demonstrated a global epidemic clade of *S. Enteritidis* enabled to become a multidrug-resistant, bloodstream-invasive infection (Feasey et al 2016, ***Nature Genetics***) and Heinz has described the emergence of the multi-resistant ST313

sublineage of S Typhimurium (Puyvelde et al 2019, ***Nat Commun***). ter Kuile has studied **MALARIA PREVENTION** strategies in pregnancy advancing understanding of field safety and efficacy (Desai et al. 2015, ***Lancet***). The **STATISTICAL DESIGN AND ANALYSIS** of clinical trials is led by Wang (Ahmed et al 2019 ***Lancet Inf Dis***).

***Tropical Disease Biology***

In the field of **MALARIA** chemotherapeutics Biagini has elucidated the long-elusive mechanism of action of primaquine (Camarda et al 2019, ***Nature Communications***) while Ward has undertaken preclinical work on novel antimalaria drug candidates (O'Neill et al 2017, ***Nature Communications***). Our understanding of the molecular pathophysiology of malaria has been advanced by Craig (Storm et al 2019, ***EMBO Molecular Medicine***) and Urban (Ogwang et al 2015, ***Science Trans Med***). Hastings uses population genetic models of infectious agents, mainly focused on malaria drug resistance (Hastings et al, 2015 ***Antimicob Agents Chemother***). In the field of **FILARIASIS** Taylor and Turner focus on Wolbachia as a therapeutic target (Taylor et al 2019, ***Science Translational Medicine***; Turner et al 2017, ***PNAS***). **SCHISTOSOMIASIS** and its vectors are addressed by Stothard (Betson et al 2014, ***J Infect Dis***). The **SNAKEBITE CENTRE** is led by Harrison and Casewell (Albulescu et al, ***Science Trans Medicine***, 2020; Yorick et al 2020, ***Cell***). Research and development of novel **DIAGNOSTICS** is the area addressed by Adams (Medley et al 2015, ***Nature***). Pleass is dissecting the roles of FcR receptors in **IMMUNITY TO PARASITES** seeking novel self-adjuvanting vaccines for the neglected tropical diseases (Blundell et al 2017, ***J Biol Chem***).

***Vector Biology***

Donnelly, working as part of a Consortium, has demonstrated the **GENETIC DIVERSITY** of one of Africa's major malaria vectors (*Anopheles gambiae* 1000 genome Consortium 2017, ***Nature***) providing new insights for the design of chemical and genetic tools. Nolan has shown how gene drives can collapse a vector population to levels that cannot support malaria transmission (Kyrou et al 2018, ***Nature Biotechnology***). The topic of **INSECTICIDE RESISTANCE** is a major feature of the Department's work; Hemingway, Ranson, Wondji and Weetman have identified new resistance mechanisms ((Vontas *et* al, 2018, ***PNAS****;* Ingham *et al*, 2019, ***Nature;*** Ibrahim et al, 2015, ***PLOS Genetics***); Paine, Wondji, Weetman and Donnelly identified the first DNA-based metabolic resistance markers for mosquitoes which providing tools to track the evolution of resistance (Riveron *et al,* 2014, ***Genome Bio***). Studies on the biology of vectors are leading to **NEW AVENUES FOR CONTROL**. Ranson has demonstrated the utility of pyriproxyfen-permethrin mixture bed-nets against malaria transmission (Tiono et al 2018, ***Lancet***) and Donnelly showed that bed-nets containing a pyrethroid synergist can reduce the prevalence of malaria in regions with pyrethroid resistant vectors (Staedke et al 2020***, Lancet)***. **INSECT BEHAVIOUR** is studied by McCall who has shown that malaria vectors are killed by small insecticidal net barriers positioned above a standard bed-net in no contact with sleepers, opening the way for deploying many more insecticides on bednets than is currently possible (Murray *et a*l 2019, ***Nature Microbiology***). Studying bloodmeal digestion in tsetse flies, Acosta-Serrano has shown that the orphan drug nitisinone is highly effective at targeting haematophagous insects (Sterkel et al, 2020, ***PLOS Biology***). Working on the **TRANSMISSION** of filariasis by mosquitoes, Reimer has demonstrated that individual and spatial heterogeneity impact disease intensity and have implications for health policy (Irvine et al 2018, ***Proc Roy Soc B***). Hughes has advanced understanding of transfer of *Wolbachia* between species, showing that the native mosquito microbiota can impede *Wolbachia* transmission in *Anopheles* (Hughes et al 2014, ***PNAS***). Meanwhile Torr, working in remote riverine settings in Africa, has shown that novel 'tiny targets' played a major role in reducing in human African trypanosomiasis incidence (Mahamat et al 2018 ***PLOS Neglected Tropical Dis***; and Stanton has developed geostatistical tools to predict the risk of human-tsetse contact (Lord et al 2018, ***J Applied Ecology***)

***International Public Health***

Jaffar and Lalloo (Director of LSTM) work on the prevention and management of **CRYPTOCOCCAL MENINGITIS** in Africa (Molloy et al 2018, **NEJM**) and how such interventions can be scaled up. Jaffar is also key to the largest cross-sectional study into emerging **NON-**

**COMMUNICABLE DISEASES** epidemic in Africa (Price et al 2018, **Lancet**) and is using skills learned in HIV research to tackle this public health threat.

**Selected illustrative major fellowships**

Ainsworth (UKRI 'Future Leaders Research Fellowship'; 2020-2024, £983,759). The aim of this fellowship is to replace crude venom in antivenom manufacture with rationally designed synthetic immunogens.

Casewell (Royal Society/Wellcome 'Sir Henry Dale Fellowship'; 2016-2021; £842,515). The objective of this project is to develop a single therapy that can be used worldwide to treat snakebite patients suffering incoagulable blood.

Jambo (MRC-DFID African Research Leader Fellowship; 2020-2023, £765,000). This fellowship will investigate the differences in immune parameters in the nose between HIV-uninfected and -infected adults, anticipating that the immune response in the nose of HIV-infected adults will be compromised.

MacPherson, (Wellcome Clinical Research Career Development Fellowship; 2017-2022, £1.13M). This fellowship asks how people with TB can be most-effectively diagnosed and linked to TB/HIV treatment. New AI software will be used to identify radiographs in Malawi that show signs of TB which will then be confirmed using point-of-care sputum tests, achieving same day-same treatment of TB.

Mwandumba, (MRC-DFID African Research Leader Fellowship; 2017-2021; £764,956). This fellowship aims to generate novel insights into control of *Mycobacterium tuberculosis* (Mtb) infection by human lung immune cells, and its breakdown during HIV-1 infection. The proposed approaches will characterise the mechanisms that underpin TB control in the lung environment.

Rylance, (Wellcome Clinical Research Career Development Fellowship; 2018-2021, £813,093). This fellowship focuses on treatment of adult sepsis in LMICs, where intravenous fluids are the primary supportive treatment but without clear understanding of their optimal use. Using both existing computational models and novel longitudinal mathematical models, the fellowship will examine the predictors of specific adverse outcomes and provided rational guidance on personalised fluid management.

Wondji (Wellcome Trust Senior Fellowship. 'Resistance escalation in malaria vectors'. £2,262,630, 2019-2024). Wondji is the first scientist based in an African country to receive a senior fellowship and have it renewed, is studying for the mechanisms of super-resistance to insecticides in malaria vectors.

**Promoting interdisciplinarity**

***Cross cutting Research Centres***

As well as their role promoting interdisciplinarity and supporting staff development, Centres help LSTM to develop new research initiatives.

The **Centre for Drugs and Diagnostics** (CDD) incorporates staff from TDB, CS and VB, and regularly works with industry, other HEIs and NGOs to discover, develop and deliver novel therapies and diagnostics. CDD has been involved in discovery and development of anti-infective compounds for 25years and now has 2 molecules in clinical development and 5 pre-clinical candidates in malaria, tuberculosis and helminths. CDD's work on COVID-19 has recently allowed *Mologic Ltd* to launch a lateral-flow test that bears the CE Mark.

The **Centre for Neglected Tropical Diseases (CNTD)** was formed in 2009 with the goal of eliminating LF through disease mapping followed by mass drug administration. CNTD is rooted in TDB but also involves staff from VB and IPH. CNTD has supported national NTD programmes in 12 countries in sub-Saharan Africa and Asia in improving their capacity for programme

implementation, laboratory facilities and diagnostic services. CNTD has also conducted monitoring and operational research into both elimination and morbidity management & disability prevention (see UOA2 ICS LSTM202).

The **Centre for Snakebite Research & Interventions** (CSRI) comprises 18 staff members from the departments of TDB, CS and IPH. CSRI facilitates discovery of novel therapeutics, clinical and public health research, postgraduate education and advocacy. See ICS LSTM103.

***Externally funded interdisciplinary awards.***

COUNTDOWN, DRUM MiRA and IMPALA, all described above, depend on wide-ranging interdisciplinary research.

**Sustainability of this UOA1 submission**

**Leadership.** The leadership of LSTM is all research active. Lalloo replaced Hemingway as Director of LSTM in 2019; these two plus Ward (Deputy Director) and Craig (Dean of Biological Sciences) are submitted here. (Squire, Dean of Clinical Science & International Public Health, is submitted to UOA2). Donnelly replaced Ranson as Head of VB in 2019 (Ranson then joined LSTM's Management Committee without portfolio), Biagini replaced Taylor as Head of TBD in 2020; Ferreira and Jaffar were appointed Heads of CS and IPH in 2018 and 2015 respectively. Since REF2014 LSTM has created Deputies to Heads of Department thereby strengthening succession planning.

**New appointments since REF2014.** The LSTM Academy is growing: the present UOA1 submission contains 54.1 FTE (compared to 31 FTE in REF2014 – a 75% increase) and includes 21 external academic appointments (38% of the present submission) made since January 2014 (for numbers in our 'Career Track' scheme – see section 2). The new appointments have enabled greater depth within research topics and strengthened expertise across the translational pipeline. All these new members of staff are principal investigators on LSTM research grants (102 grants between them totalling £45.4M). Research income is presented in detail below but there is a year-on-year trend for income per FTE rising from £451,804 in 2013-14 to £953,517 in 2019-20.

**Future goals for research and impact**

LSTM has no stand-alone 'system' to enable Research Impact: *all* our research, whether single-discipline or interdisciplinary, aims to achieve impact for the world's poorest people through translation and implementation. Knowledge exchange activity is embedded within all Departments with 29 staff engaging in consultancies worth £98.7M over the census period; £21.5M was received from industry. As signatories of the Knowledge Exchange Concordat, we are equipping our staff and students with the necessary skills and knowledge to thrive in an open research environment.

While much of the translation reported in this UOA1 submission comprises 'bench to people' (see ICS LSTM101, LSTM203 and LSTM104) UOA1 staff also work on the delivery of research in practice and changes in policy (as evidenced in all 5 of our ICS). Our ambitions will be taken forward by continuation of our high success rate in grant applications, and through leverage of our *Strength in Places Fund* award (see section 4) which will benefit all 4 Departments.

**Department of CS** plans expansion of its work in *Human Infection Challenge Models* (both UK and overseas) and is building on existing work to address antimicrobial resistance (e.g. MRC/DFID DRUM consortium (above) and the Fleming Fund work examining AMR in Uganda and Malawi). LSTM has a critical mass of global health focused respiratory physicians who are leading programmes of work in Africa addressing major respiratory related causes of morbidity and mortality across the life course including sepsis, pneumonia in the under 5s, TB, chronic respiratory diseases and the adverse health effects of exposure to household air pollution. CS is

also expanding research on Global Child Health, particularly in nutrition, aiming to move into large cohort studies embedded with Health and Demographic Surveillance Sites.

**Department of TDB** plans to remove traditional disciplinary silos within the department and extend its successful transdisciplinary collaborative models, operating across the translational T1-T4 continuum, to address major human infections and unmet global health challenges. It will do this through the strategic expansion in researchers, infrastructure and partnerships. Expansion of Hazard Group-3 Pathogen Translational Platforms is planned to support research of new therapeutics, vaccines and diagnostics, as well as basic studies of disease pathogenesis, immunology and drug resistance. Translational research is collaborative by definition and the department's major achievements have always been delivered through partnerships. TDB currently operates in over 50 countries, predominantly LMICs, and plans to continue to expand this strategic network with key academic and non-academic partners that share its vision, including governmental, non-governmental organisations (NGOs), product development partnerships (PDPs) and industry (large pharma and SMEs).

**Department of VB** has recently expanded its portfolio in vector control trials for malaria and NTDs and this is a clear area for growth as evidenced by the appointment of a spatial epidemiologist and a trials specialist and greater integration with activity in the Department of CS. Trials of new interventions targeting the mosquito vectors of malaria with clinical endpoints are planned for the Democratic Republic of Congo, Uganda, Kenya and Tanzania and these will be followed by an extension into arbovirology with CS staff. Key strengths in insecticide-based vector-borne disease control will be enhanced by novel transgenic technologies which we would expect to move to near field trials within 5 years. VB also plans growth in applied genomics and genomic epidemiology, an initiative which includes staff from across LSTM. Underpinning much of the translational work will be the '*innovation-2-impact'* programme' which interfaces with in-country regulatory authorities, and our key relationships with the IVCC and industry partners.

**Department of IPH** will continue to expand its clinical trial work on HIV and its related pathogens. In the area of chronic diseases, IPH will continue to evaluate the transformation of health services to provide integrated services, both at the health facility and the community level, with a particular focus on preventing the very high and increasing mortality associated with diabetes and hypertension. (The plans of IPH in other research areas are submitted to UOA2).

**2. People**

**Staffing strategy and staff development**

**Aims and guiding principles**

LSTM aims to achieve depth of research excellence within its range of interests and is committed to hiring and promoting only the very best academic staff, irrespective of gender, ethnicity, or nationality (subject to UK Visas & Immigration controls). The Management Committee (MC) of LSTM has responsibility for policy, but the recruitment process and responsibility for staff development are devolved to Departments. Joint appointments between departments are encouraged.

LSTM conducted a formal review of its research culture during 2019-2020, particularly **researcher careers** and **researcher assessment** which overlap both one-another and changes to **research integrity**. Working Groups (inclusive of post-docs, technicians, programme managers and academics) conducted 'gap analyses' and made recommendations to MC. A continuous cycle of review (including open consultation with staff) has been instituted and the Board of Trustees will be briefed regularly on progress. Following these recommendations, LSTM has signed up to: (**A**) The revised ***Vitae Researcher Development Concordat***. Changes are being implemented that include: (i) Involvement of researchers in development and review of policy; (ii) A systematic approach to workloads; (iii) A revised programme of training for line managers (including mental health awareness); (iv) An institution-wide review of job security; and (v) Formalisation of career advice (including opportunities to move into sectors other than

Higher Education). (**B**) The ***San Francisco Declaration on Researcher Assessment*** (**DORA**). Changes are being implemented that include: (i) A rolling programme of presentations on research performance expectations (the details of which were published in intranet pages in 2016); (ii) Clarification of those 'wider contributions' approved by LSTM; (iii) Greater transparency in the assessment of candidates for appointment and promotion; (iv) The investigation of DORA-related complaints; and (v) A rolling programme of monitoring compliance with DORA principles. (**C**) The revised ***Universities UK Concordat on Research Integrity***. Changes are being implemented that hinge on: (i) rolling training programmes in laboratory work (including work on animals), work on human subjects and systematic reviews; and (ii) development of a proactive system to ensure that the highest standards of research integrity are maintained.

**Recruitment**

**Posts funded from LSTM core budgets.** 21 of 54.1 FTE (39%) submitted to UOA1 are new external academic appointments to 'research-&-teaching' contracts during the Census Period (ranging from Lecturer to Reader). A further 10 internal academics moved onto substantive positions as part of our Career Track process, which underwrites salary support for promising researchers and provides mentorship to help them transition to permanent contracts. In addition, 29 academics have been promoted internally within UOA1 (on 'research-&-teaching' contracts ranging up to Professor).

**Posts fully supported from external funding sources.** 3 of 54.1 FTE (5.5%) submitted to UOA1 (all on open-ended contracts) are fully supported by external funding. Since 2019, and responding to a call from staff, a concerted effort has been made to reduce the use of fixed term contracts for 'R-only' staff by engagement with line managers (to identify upcoming vacancies) and with staff (to explore their career plans). Staff eligible for redeployment are then prioritised for consideration for roles ahead of other applicants. As a result, across the whole of LSTM in the present Census Period, 33 of 139 staff on research-only contracts have changed from 'fixed term' to 'permanent subject to funding' contracts'.

**Support and training**

**Support for Early Career Researchers (ECRs).** ***(A) The Wellcome Trust Institutional Translational Partnership Award (iTPA)*** (£600k, 2020-2022) will allow LSTM to overcome barriers experienced by staff that feel limited in their ability to undertake translational research. Several "vehicles" have been established: (i) Senior Translational Priority Fellowships to support mid-senior level researchers giving them time and resource to address barriers in translating their research; (ii) an "Enabling fund", to support small requests to accelerate translation of basic findings; (iii) an "Internship Fund", targeted at ECRs to support staff in gaining vital experience in industry/non-academic organisations, (iv) "Translational Training", bespoke workshops to assist with T1-T4 knowledge/activities. ***(B) Internally funded schemes*** (i) The *Director's Catalyst Fund*, launched in 2016, with Wellcome Trust Institutional Strategic Support Fund (ISSF) support, provides grants of up to £50K to accelerate the careers of early career researchers and support external grant applications: 21 awards have been made to date, 3 of which have directly resulted in external fellowships (Ainsworth, Future Leader Fellowship ;Grigoraki, Wellcome Henry Dale Wellcome Fellowship; Kondwani African Research Leader). (ii) *Seed Funding* to support innovation and proof-of-concept is available to researchers within LSTM through activities including the MRC-funded *Confidence in Concept* and *Proximity to Discovery Awards* (see below under 'Collaborations'). ***(C) The MRC Skills Development Fellowship Programme in Translational and Quantitative Skills for Global Health*** is described in detail below.

**Support for overseas based staff.** Long-term placements in LMIC are essential to our mission. Thirteen UOA1 staff (24%) are based overseas in Malawi, Kenya, Cameroon, Nepal and Uganda (see Figure 3). We support these staff by maintaining high-specification laboratory/clinical research environments (e.g. MLW and Centre for Research in Infectious Diseases (CRID) Programmes; see below), by facilitating integration with UK-based colleagues

and by provision of personal financial support (to offset higher tax rates, security fees, housing costs, health insurance and flights). This support has helped several of our overseas staff win prestigious Fellowships in the current Census Period (Wondji, MacPherson, Jambo, Mwandumba and Rylance; see above).

**Medical staff**. Twelve UOA1 staff (21%) hold honorary consultant contracts with NHS Trusts or *Public Health England Northwest* and provide clinical services in Merseyside. In addition, many staff have health service roles overseas as part of their placements with partner organisations (e.g. the *Queen Elizabeth Central Hospital*, Malawi). All these staff have carried extra service duties during the 2020-21 COVID-19 pandemic. In partnership with UoL, LSTM has held a '*Wellcome Trust Clinical PhD Programme in Health Priorities of Resource Limited Settings'* since 2007. This funds four 4-year Fellowships per annum with a total grant award of £5M to LSTM over the census period (and an identical sum to UoL). 26 young doctors have started these highly competitive Fellowships in the present Census Period of whom 13 are (or have been) registered for PhDs at LSTM. There is an impressive record of retention in academia: 5/13 Fellowships have completed and remain employees of HEIs, 5/13 are ongoing and 3/13 have completed and returned to NHS employment. Four past Fellows (Feasey, Fletcher, MacPherson and Rylance) now hold substantive academic posts at LSTM and are included in the present submission.

**Training for researchers**. The staff development programme includes technical, transferable skills, teaching and management courses. Research staff can take courses from our MSc programmes to update their knowledge. LSTM is a signatory to the *Technician Commitment, Knowledge Exchange Concordat* and the *Vitae Researcher Development Concordat* (see above)*.*

**Opportunities for teaching qualifications**. Since 2014, 28 staff have completed the *Professional Certificate in Supporting Learning* (accredited by the 'Staff & Educational Development Association'). Since 2019, 19 staff have completed the *Leading in Global Health Teaching* scheme (accredited by 'Advance-HE'); this qualification gives the opportunity for staff to be awarded different categories of Fellowship of the Higher Education Academy.

**Appraisal.** All research and academic staff are formally appraised annually by senior members of their Departments. Academics who hold Honorary Consultant Contracts in the NHS also undergo an annual joint NHS/LSTM appraisal. An LSTM Workload Dashboard is currently being trialled that will provide up-to-date data on activity to allow transparent and fair discussions.

**Research students**

Two points should be stressed at the outset: (a) LSTM won degree awarding powers in August 2017 and began to register PhDs soon after. Numbers of students are projected to rise as numbers of Masters students double between now and 2024. (b) In line with its Mission, 34% of current LSTM-registered postgraduate students are based overseas (and thus excluded from the REF).

Research students are fully integrated into research groups. An annual postgraduate symposium provides an opportunity for all students to present their work. Students undertake an appraisal of their training needs annually using the 'Development Needs Analysis' (DNA) tool and engage with training opportunities via the PGR Skills Development Programme (SDP), MSc modules, and external courses. DNA and SDP are built around the domains of the VITAE Researcher Development Framework. LSTM consistently achieves approval scores from student participants of above 80% in the Postgraduate Research Experience Survey (PRES) in relation to Professional Development and Research Skills.

Each student has at least two academic supervisors and is also supported by a 'Progress Assessment Panel' (PAP). The PAP comprises two academics who monitor the student's progress and make recommendations on the project, supervision, and pastoral issues. Annually,

students produce a portfolio of work to evidence their progression and present this to the PAP. The PAP produces a report for the Director of Postgraduate Research containing recommendations relating to continued registration.

The MLW programme holds a training budget from the Wellcome Trust (directed by Jambo) which supports pre-MSc 'interns' (totalling 35 2018-2020), MSc students (36 in the same period) and PhD students (44 in the same period, none of whom may be submitted to the REF).

**Numbers and funding sources**
Growth in UK Postgraduate training has been a strategic priority for LSTM since the award of HEI status in 2013 and is a growing component of our research and scholarly activity. Of the 109 doctorate students who have registered since August 2013, 86 had an UOA1 staff member as primary supervisor and 33/86 students were non-EU. Gender was declared by all students: 46/86 female and 40/86 male. Ethnicity was declared by 83/86 students: 41/83 were BAME and 42/83 were white. During the period August 2013 to July 2019 the completion rate (full- and part-time) was 97%.

***MRC Industrial Collaborative Awards in Science and Engineering (CASE) and Doctoral Training Partnership (DTP) scheme.***
Funding was awarded in 2015 to establish a PhD programme with a focus on training the next generation of leading scientists in translational and quantitative skills for global health for the benefit of the world's most vulnerable people and communities. The programme attracted an additional funding stream from the MRC in 2017 as part of the 'National Productivity and Investment Fund'. The programme comprises a one-year full-time MRes in Global Health (taught at **Lancaster University**) followed by a 3-year full-time PhD at LSTM. Emphasis is placed on both leadership in translational research and the quantitative and interdisciplinary skills needed to 'bridge' across the traditional phases of translational research and the aim is for graduates to progress to high-profile roles in academic, industry, and policy settings. 30 students are currently registered in the programme. Three of the five fellows in the first cohort have now achieved either academic posts or funded fellowships.

**Equality and diversity**

LSTM is committed to inclusivity for the diverse population for whom and by whom our activities are delivered. LSTM invested dedicated *Equality, Diversity & Inclusion* (E,D&I) resources in 2016, including a full-time post for development of the E&D strategy. E&D strategy is governed by the *Equality, Diversity & Inclusion Committee* (EDIC), which is co-chaired by the LSTM Director and Global Director of HR. EDIC consists of Equality Champions from faculties and professional support functions, representation from staff networks and student community. EDIC reports to Management Committee and Board of Trustees.

The E,D&I strategy addresses *Equality Impact Assessment* processes, governance structures and data capturing. Anonymous shortlisting and gender decoding software, review of career progression mechanisms and a new *Dignity at Work* policy all contribute to minimise recruitment bias. All staff are required to complete mandatory E,D&I e-learning at induction and at regular intervals. LSTM has an online reporting platform, *Freedom to Speak Up*, where people can raise issues relating to safeguarding, staff and student conduct (including allegations relating to research integrity and DORA) and wellbeing. Following staff feedback, further information relating to racism and racial harassment has been added to the system to raise awareness and encourage reporting of these issues.

2019-20 has seen the creation of two staff-led networks; the LGBTQ+ Network (open to both staff and students) and our BAME Staff Network. Events of May 2020 highlighted ongoing inequality across the globe: LSTM was challenged by staff on adequacy of its focus on internal race equality and a Taskforce is now addressing key areas in consultation with the BAME Staff Network. Outputs from the Taskforce will feed into the new 2021-2024 ED&I Strategy and will work to ensure that LSTM becomes an actively anti-racist Institution.

LSTM holds two faculty-level Bronze Athena SWAN awards and institutional-level Bronze. Advance HE (the awarding body) has offered all institutions a 12-month extension to current awards because of COVID-19, and LSTM will submit an institutional-level bid for Silver in April 2022, having undertaken a thorough self-assessment.

LSTM has created an intranet wellbeing hub (including links to external organisations) to provide support and raise awareness (e.g. mental health awareness and stress awareness days). A global employee assistance programme has been started, which allows access to counselling support.

Criteria and processes for promotion to academic roles have recently been updated: Teaching-Only and Research Only routes to progression have been formed and work has started on a career development framework for Programme Management roles. The Technician Commitment action plan is being implemented and promotion opportunities in professional services will shortly be updated.

COVID-19 has posed unprecedented challenges. 50 people were placed on furlough: fewer than 5 of these have left LSTM. More than 30 staff were seconded to support the NHS or Public Health England. A 'pulse survey' was done in May 2020 to determine impact of COVID-19: over 60% of responders rated their wellbeing as 'good' or 'very good' and 80% felt supported by their managers.

**Capacity Strengthening**

LSTM has supported multiple overseas staff to gain independent fellowships. Thirteen Wellcome Trust *'Public Health and Tropical Medicine Training and Intermediate Fellowships'* and 22 '*Master's Fellowships in Public Health and Tropical Medicine'* were sponsored by LSTM academics in the Census Period. The '*Partnership for Increasing the Impact of Vector Control'* (PIIVeC) programme supports fellowships for 12 African postdoctoral research fellows, who in turn manage 15 junior scientists, working on the control of vector borne disease. LSTM has also supported two people submitted to UOA1 to secure African Research Leadership awards: Jambo and Mwandumba (both in the MLW Programme). Additionally, capacity development is imbedded in our collaborative projects (see below).

LSTM believes that academic support is insufficient, on its own, for the capacity development of talented researchers: attention is also needed to governance aspects of the local environment. With this in mind, the Head of Research Management Services (RMS) was a member of the technical committee to establish the 'Good Financial Grants Practice (GFGP) Accreditation Scheme' and is now a continuing member of the GFGP Scheme Governance Committee. Centre for Sexual Health and HIV AIDS Research (CeSHHAR) has recently become the first organisation in the world to be awarded gold level GFGP accreditation, and LSTM is currently undergoing platinum level GFGP accreditation so that we can be the leading exemplar across the global grant community.

## 3. Income, infrastructure and facilities

Research income per FTE per annum shows a clear upward trend. It must be remembered that income in the year 2019-20 has been affected by COVID-19:

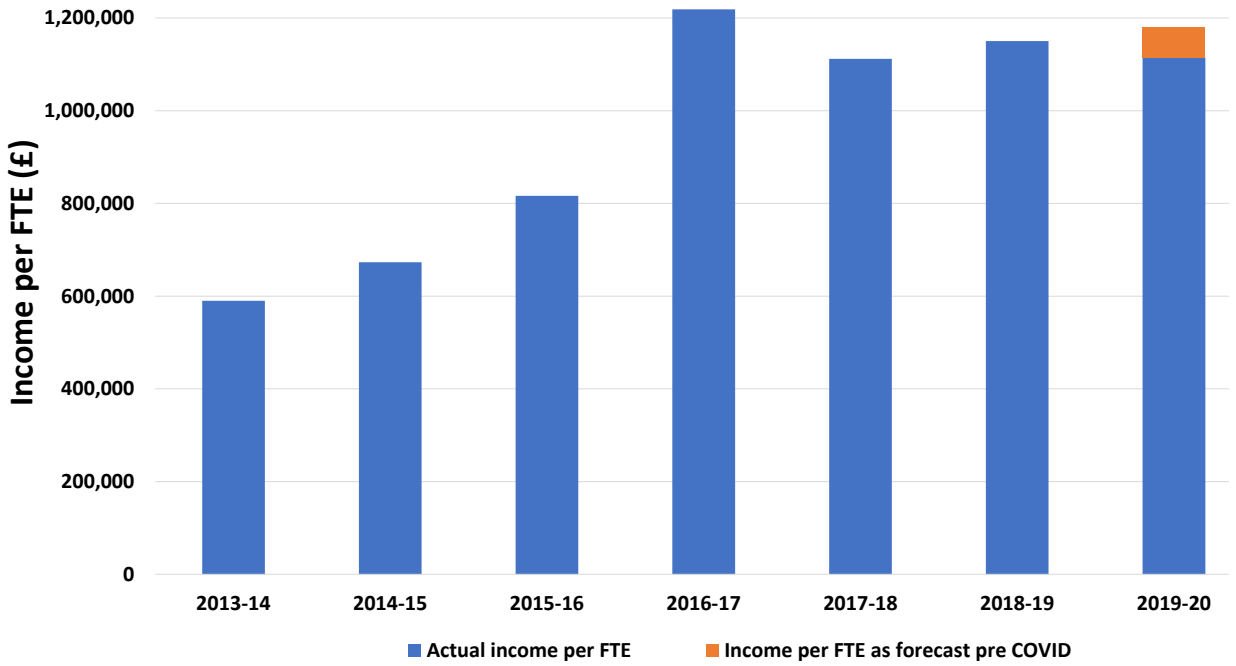


**Figure 1. Income per FTE per annum (inclusive of partner income).**

The average research income per FTE per annum over the whole Census Period was more than double that in 2014: £953,517 compared with £451,804 in 2014.

LSTM seeks to maintain and build a diverse portfolio of funding as illustrated in Table 1:

**Table 1: Major sources of grant income over the census period.**

| | UKRI | UK charity | UK gov | EU gov | Non-EU charity | Other non-EU |
|---|---|---|---|---|---|---|
| Total award (millions) | £34.1 | £89.6 | £70.6 | £20.2 | £93.4 | £31.8 |

Unsurprisingly, given its previously low relevance to LMICs, NIHR has not been a major source of funding for LSTM but the *Global Health Research Units and Groups Scheme* started in 2017 and awards totalling £17.7M have been won (income from these has started to appear recently).

## Infrastructure and facilities

### Buildings

The LSTM campus is adjacent to both UoL and the Liverpool University Hospitals NHS Foundation Trust (LUHFT).

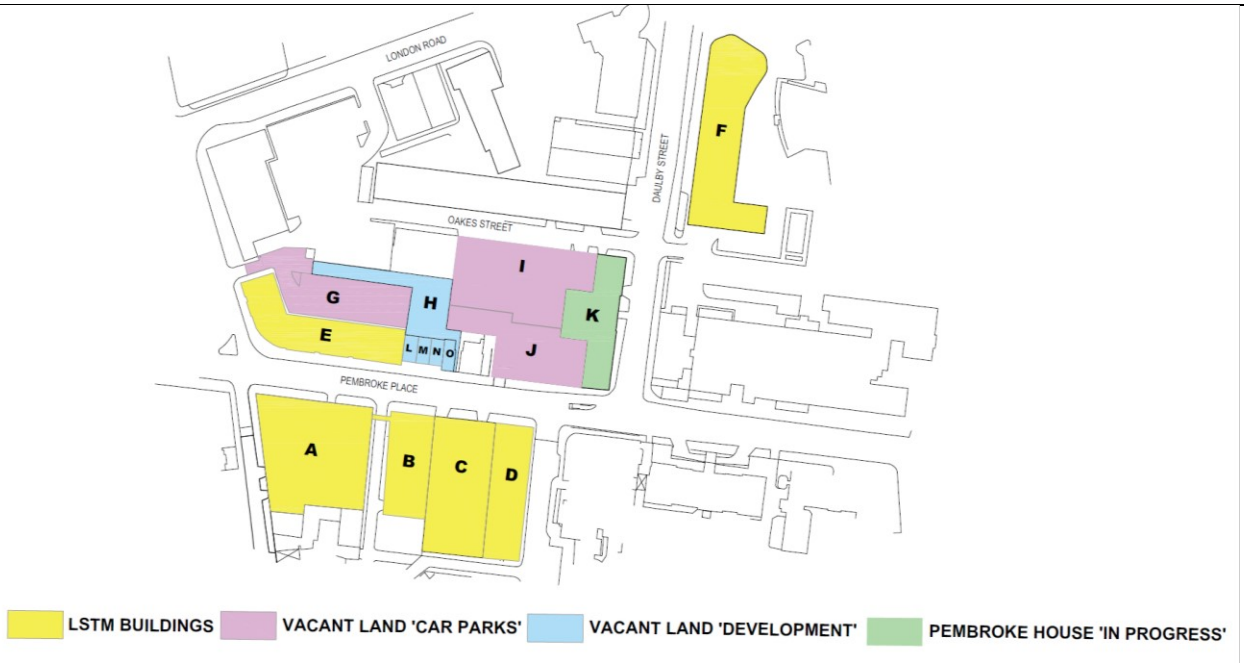


**Figure 2. The LSTM Campus.**

**The Liverpool campus at REF2014**. The *Centre for Tropical Infectious Diseases* (CTID; 8,707m; A on map), which is contiguous with the original Maegraith, Gilles and Kingsley buildings (B, C, D; 7,300m$^2$ in total), was opened in 2009.

**New buildings since REF2014**. The *Wolfson Building* (E; opened 2015; £8.8M; 2,800m$^2$) is 50m from CTID and is designed to support later stages of translation and interdisciplinary activities (including the *Innovative Vector Control Consortium* (IVCC) see below). The *Liverpool Life Sciences Accelerator Building* (F; 'the Accelerator') is a partnership with LUHFT and sits within the hospital grounds 150m from the CTID. The *Accelerator* (2017; £25M; 7,230m$^2$) houses LSTM's Human Challenge facility, Hazard-Grade-3 microbiology, parasitology and insectary facilities. Importantly, the *Accelerator* also houses SME companies as part of the *Knowledge Quarter* development (see section 4).

**Land bank in Liverpool.** LSTM has secured a 3497m$^2$ land bank that is contiguous with our other buildings and LUHFT to accommodate future expansion plans. Current planning builds upon our recent *Strength in Places Fund* award for which we envision a Translational Infection-Research Facility in collaboration with Liverpool City Region (see section 4) and a major new teaching hub in a refurbished *Pembroke House* (K).

**Buildings in the Malawi-Liverpool-Wellcome Programme (MLW)**. LSTM investments in buildings at MLW are described in section 4.

**Governance and administration**
LSTM Board of Trustees interacts with academics and receives reports from the Management Committee (MC chaired by the Director). MC steers LSTM determines strategy and controls the budget (including elements of strategic investment including the Wellcome Trust *ISSF* (currently £1.2M over 5years). Research Committee, like other committees, reports to MC, advises on research strategy and makes strategic investments in people (including bridge funding, the Director's Catalyst Fund and Jean Clayton awards). The Director is represented on the *Health & Life Science Board* of Liverpool City Region and the *Liverpool Health Partners Board*.

**Supporting basic science and translation**
**Laboratories.** LSTM has 28 HAZARD-GRADE-3 (HG3) laboratories (the highest density of such labs in one location in UK academia) and a HG3 insectary. There is a dedicated CHEMISTRY Laboratory with robotic *High Throughput Screening* housed in HG3-containment. This allows whole cell (pathogen) screening (again unique within the UK academic sector). A state-of-the-art

analytical laboratory supports drug metabolism and pharmacokinetic studies from lead optimisation to clinical trials as well as proteomic and metabolomic studies. CTID also houses a HG3-IMAGING suite with stand-alone confocal and high-content screening platforms with flow cytometer/cell sorter. LSTM hosts a UK Home Office accredited HERPETARIUM containing the largest and most diverse collection (>200) of venomous snakes in the UK. With eight 19m$^2$, six 13m$^2$ and a further eight smaller temperature and humidity-controlled rooms, LSTM also has the largest collection of INSECTARIES in the UK. In addition, we have bespoke laboratories for measuring insect behaviour, including facilities to record insect nocturnal flight using infrared cameras, flight mills, and specialist equipment to dispense insecticides onto a variety of surfaces ranging from microliter dispensers to whole room sprayers.

**Animals.** LSTM acquired a Home Office Certificate of Designation for animal research in 2010. This includes a dedicated animal experimentation facility and the herpetarium (above). Supported by access to UoL's Biomedical Research Unit, this facility underpins the development and use of animal models to (i) better understand the pathophysiology of several NTDs and (ii) preclinically test the efficacy of new treatments. LSTM's Animal Welfare & Ethics Review Board governance ensures that this clinically important research is undertaken using protocols that maximally implement the 3Rs (*Replace*, *Reduce and Refine* the use of *animals* for scientific purposes), and that our publications follow ARRIVE (Animal Research: Reporting of In Vivo Experiments) guidelines to provide maximum benefit to the research community.

**Clinic.** The Department of CS collaborates extensively with the LUHFT Clinical Research Facility where early phase clinical trials may be conducted on NHS patient volunteers. In addition, the adjacent *Accelerator* (see above) houses LSTM's Human Challenge facility in which human challenge model and vaccine trials are undertaken. (Clinical studies in LMICs are based in overseas programmes, described below).

**Clinical Trials.** The Global Health Clinical Trials Unit (GHTU) includes twelve staff members with expertise for designing, supporting and managing Phase 2 and 3 randomised and observational studies in low-income settings. Most of these studies are conducted by LSTM and its partners, but we also work on external trials that fit within LSTM's vision and strategy. Current trials address the prevention of post-partum sepsis 'BabyGel'; prevention of mother-to-child transmission of HIV 'DolPHIN 2'; malaria chemoprevention for severe childhood anaemia 'PMC study'; treatments for malaria, sexually transmitted and reproductive tract infections in pregnancy (IMPROVE 1 and IMPROVE 2); new treatments for cryptococcal meningitis (AMBITION); diagnostics tools for COVID-19 (Faster Dx) and COVID-19 outcomes in people with HIV (CO-HIVE).

The **Research Computing Unit (RCU)** includes two core funded staff dedicated to developing and deploying biomedical computing. The RCU provides computational resources for image processing, high content screening, gene and protein identification, bioinformatics analysis and software development including a custom-built scientific linux desktop coupled with high performance computing facilities. The RCU also promotes knowledge exchange and secondary exploitation of data by providing infrastructure and research support to convert algorithms into more accessible and user-friendly tools and web resources for use by the community. Notable examples of freely available tools include the insectiside resistance explorer (IR-Tex), the transcriptome assembler VTBuilder and MAP-interface-comparison (which received second place in the Wellcome Data Re-use Prize: Malaria in 2019). RCU and GHTU have joined up with our data governance office to establish a Centre for Data, to support the management and analysis of data by researchers in LSTM.

**Research governance**
The Research Governance Manager (RGM) is responsible for ensuring that research is undertaken to the highest standards in accordance with UK law and the LSTM's *Guidelines on Good Research Practice*. The *Guidelines* follow national guidance from Universities UK and the UK Research Integrity Office and are supported by detailed policies for ethics review, health and safety, grant management, research management, confidentiality of data and records,

intellectual property, working with the private sector, and investigating allegations of misconduct. These policies have recently been reviewed to ensure conformity with the UUK Concordat for Research Integrity. The Research Ethics Committee (REC) reviews all protocols for work on human participants in LMICs including (but not restricted to) randomised trials (including those on investigational medical products) and observational studies (including those using social science methods). The expertise of LSTM REC is recognised by the frequent requests to review protocols from other UK Institutions (e.g. Marie Stopes UK, Consultancy Companies, other HEIs and MRC) for studies to be conducted in LMICs. The LSTM REC also reviews protocols for work being conducted in the UK by LSTM researchers that does not fall within the remit of the HRA/MHRA. Finally, the *Research Governance Oversight Committee* is responsible for oversight of work on human subjects, has a detailed audit schedule and conducts ad-hoc audits as required.

**4. Collaboration and contribution to the research base, economy and society**

**Leadership of national and international consortia**

LSTM UOA1 staff have led 12 collaborative awards (of >4 partners and value >£2.5M) in the Census Period and examples are described below.

**The Anti-Wolbachia Consortium (AWOL).** AWOL is described above but here we set out the range of scientists and partnerships that contribute. AWOL needs expertise in parasitology, pharmacology, mathematical modelling, and medicinal chemistry (UoL). This team enables in house synthesis and assessment of novel compounds. AWOL is in partnership with the following companies: Abbvie, Astra Zeneca and Eisai, and collaborates with the following HEIs: Universities of Buea, Bonn, California San Francisco and Texas (Medical Branch).

**The Partnership for Increasing the Impact of Vector Control (PIIVEC).** Many diseases of LMICs are transmitted by insect vectors and PIIVEC is a UKRI-GCRF supported collaboration that brings together researchers and policy makers to stimulate the vector control research pipeline. PIIVEC invests in promising future leaders, filling knowledge gaps, and the sustainable use of evidence in decision-making. PIIVEC focuses on three countries with high burdens of vector-borne disease: Burkina Faso, Cameroon and Malawi.

**Snakebite**. LSTM partnered with two major antivenom manufacturers (MicroPharm Limited, UK and Instituto Clodomiro Picado, Costa Rica) to design, clinically test and deliver two new, cost-effective, life-saving treatments for countries in West Africa (see ICS LSTM103).

**Malaria in pregnancy** is one of the leading causes of adverse pregnancy outcomes. Current control strategies are under threat due to increasing drug resistance and suboptimal coverage with existing tools. LSTM has been the coordinating centre of the BMGF-EU-funded '*Malaria in Pregnancy Consortium'*, a network of 40 research institutions, that aimed to improve the control of malaria in pregnancy. Research led by LSTM, consisting of meta-analyses, observational studies and multicentre trials, has contributed directly to WHO and endemic country policies (see ICS LSTM104).

**MRC Confidence-in-Concept (CiC) and Proximity-to-development (P2D**). LSTM has partnered with the London School of Hygiene and Tropical Medicine, the Jenner Institute at Oxford University and Public Health England to form a translational partnership dedicated to reducing the burden of tropical infectious diseases. Some 90% of CiC-P2D projects are in partnerships with industry and in collaboration with consortium partner institutions. *Researchfish* data indicates that CiC-P2D has leveraged ~£45M in follow-on funding and directly contributed to 1 spin-out company (linked to Oxford), 15 patent applications and 1 trademark.

**Strength in Places Fund award – 'Delivering Integrated Solutions for Human Infections'.** This £18.6M UKRI award (made in 2020 and led by Hemingway) gave the leverage needed to form the *Infection Innovation Consortium* (iiCON) the North West's largest concentration of infectious diseases research in a new £120M programme. iiCON will capitalize on the region's

track record in working on translational programmes in vaccines, diagnostics, therapeutics and antiviral formulations. The Consortium will deliver economic and regional productivity by creating eight specialist commercially sustainable research platforms for infectious disease therapeutics in North West England. At the core, safe, effective and flexible human organoid and 'human challenge models' and associated technologies will reduce the risk of late stage failures of new therapeutics. Core Consortium partners**:** UoL, the AMR Centre, Unilever, LUHFT, and Evotec.

**Responsiveness to emergencies and emerging risks**

**The COVID-19 pandemic**
**Leadership.** (a) Lalloo chairs the Department of Health and Social Care (DHSC) COVID Prophylaxis Advisory Group and has had advisory roles on the *Scientific Advisory Group for Emergencies* (SAGE) and Advisory groups for DFID. (b) Fletcher was seconded to WHO (Geneva) as part of the 'clinical characterisation and supportive care R&D team'. Fletcher also led the WHO research team deployed to South Korea.

**COVID-19 therapeutic and vaccine studies**. In collaboration with UoL, LSTM investigators were awarded £15,879,000 over the course of 2020 (by the Wellcome Trust, the Steve Morgan Foundation, MRC, UNITAID and GlaxoSmithKline (GSK)) as part of the AGILE-ACCORD platform to study multiple candidate agents for the treatment of COVID-19. Ferreira is a member of the National NIHR COVID-19 Vaccine Research Delivery Group and under her leadership Liverpool was the top recruiting site in the UK to the Phase-3 trial of the Oxford-AZ vaccine; she also led two additional Pfizer COVID-19 vaccine studies.

**COVID-19 diagnostics.** Adams worked with *Mologic Ltd* (London and Boston) and St George's University of London to develop a 'triple antibody' lateral flow test that was granted a CE Mark and is now commercially available.

**The Malawi COVID-19 pandemic**. The MLW programme has had a national leadership role and has taken practical measures to save lives. MLW was awarded a £2.55M 'emergency response grant' by the Wellcome Trust having identified oxygen provision (there was almost no availability) and diagnostic testing as priorities. MLW committed £1M each to purchase of personal protective equipment and to establish an oxygen concentration plant at Queen Elizabeth Central Hospital (QECH) (the national tertiary-referral centre). This permitted establishment of a Respiratory High Dependency Unit at QECH – the only such facility in Malawi. A further £300K of the award (in collaboration with UoL) established provision of COVID diagnostics.

**Responses to other emergencies**
**Ebola** – (a) Jacob and Fletcher led the WHO 'clinical response team' in Guinea, Sierra Leone and Liberia and drove a paradigm shift in supportive care delivery. (b) Jacob and Fletcher were also both members of the WHO expert panel for Ebola supportive care guidelines. (c) Jacob was deployed by WHO to lead the 'Monitored Emergency Use of Unregistered and Investigational Interventions' (MEURI) trial in the Democratic Republic of Congo. (d) Lalloo was a member of SAGE and chaired major clinical trials committees assessing Ebola treatments.

**Crimean-Congo Haemorrhagic Fever (CCHF).** Fletcher was a member of the WHO (Geneva) CCHF 'research & development taskforce'.

**UK Public Health Rapid Support Team.** Fletcher was Co-PI of this UK-Aid-funded project to investigate outbreaks of undifferentiated febrile illness in Sudan and led the 2018 investigation of the Chikungunya outbreak in Africa.

**Well-Travelled Clinics Ltd** (**WTC**) is a not-for-profit LSTM company that provides specialist travel and occupational health services to the public and corporate clients. WTC is the healthcare supplier for the *UK Emergency Medical Team*, *Concern* (an Irish NGO), the *Mines*

*Advisory Group*, and Médecins Sans Frontières (MSF) (in conjunction with the Hospital for Tropical Diseases in London). In 2014, WTC set up mobile clinics to support the rapid pre-deployment and post-deployment readiness of over 200 *UK Emergency Medical Team* health care workers to Sierra Leone for the Ebola crisis. In 2018, WTC provided emergency pre-deployment and post-deployment support to several NGOs to the diphtheria outbreak in Bangladesh (which again involved mobile clinics). More recently, WTC has supported the deployment of NGO teams to Zambia, Bangladesh and Yemen during the COVID-19 pandemic. WTC nurses and staff were seconded to the Clinical Research Network from the start of the COVID-19 pandemic to support the COVID research response. They played a crucial role in recruitment to the Oxford-AZ vaccine phase-3 in Liverpool (see above).

**Shared knowledge: strategic collaborations in the north west of England**

**Liverpool City Region Combined Authority (LCR)**. LCR makes investments across 6 local authorities in areas such as transport, employment, culture, digital technologies and housing. LCR's devolved powers make it a focus for local collaborations with HEIs. LSTM had a pivotal role in LCR's submission to the Department for Business, Energy and Industrial Strategy (BEIS) *Science & Innovation Audit* (2018), and LCR provided support for the LSTM's successful *Strength in Places* Fund application.

**The Knowledge Quarter (KQ)**. KQ aims to make LCR a focus for innovation and is the single point of contact for investors. KQ is steered by a 'special purpose vehicle', the KQ Development Company which generates £1billion in income per year and supports 14,000 full-time jobs. LSTM is a partner-member of the KQ Board.

**Liverpool Health Partners (LHP)**. LHP is the academic health science system in Liverpool City region and LSTM is one of its founder-members. LSTM and UoL are collaborating with LHP in the development of a Biomedical Research Centre application for 2021. At the time of REF submission, LHP is Coordinating the Liverpool research response to COVID-19 by prioritising and streamlining regional efforts in COVID research and engaging businesses developing COVID-19 products / services. LSTM's Department of CS has active engagement with LHP for delivery of phase III trials of COVID-19 vaccines.

**CEIDR** is a partnership with UoL which promotes links between academic groups and industry to advance drugs, vaccines and diagnostics towards market.

**Innovation in partnership with industry**

**The Innovative Vector Control Consortium** (**IVCC**). LSTM's links with industry and *product development partnerships* (PDP) are wide but the largest is with IVCC, the only PDP working internationally in vector control. IVCC was established in 2005, through a $50M grant to LSTM from BMGF. Since January 2014 IVCC has won a further £214M in external grants and contracts. IVCC works with stakeholders to facilitate the development of novel interventions and brings together partners from industry, the public sector and academia and benefits from technical expertise in vector control from the VB department.

**Liverpool Insect Testing Establishment** (**LITE**). LITE accelerates the search for new public health insecticides in cooperation with IVCC. LITE provides technical services to industrial partners (including Syngenta, Bayer, Mitsui AgroChemical, Sumitomo and BASF) to screen new chemicals including new insecticides or repellent based products using a variety of biological assays against a wide range of mosquito populations. LITE houses many colonies of insecticide-resistant and susceptible mosquito strains that have been characterised phenotypically and genotypically. All testing is performed to standard operating procedures and the Medicines and Healthcare products Regulatory Agency (MHRA) accepted LITE to the *Good Laboratory Monitoring Authority* programme in March 2020.

**Worldwide collaborations**

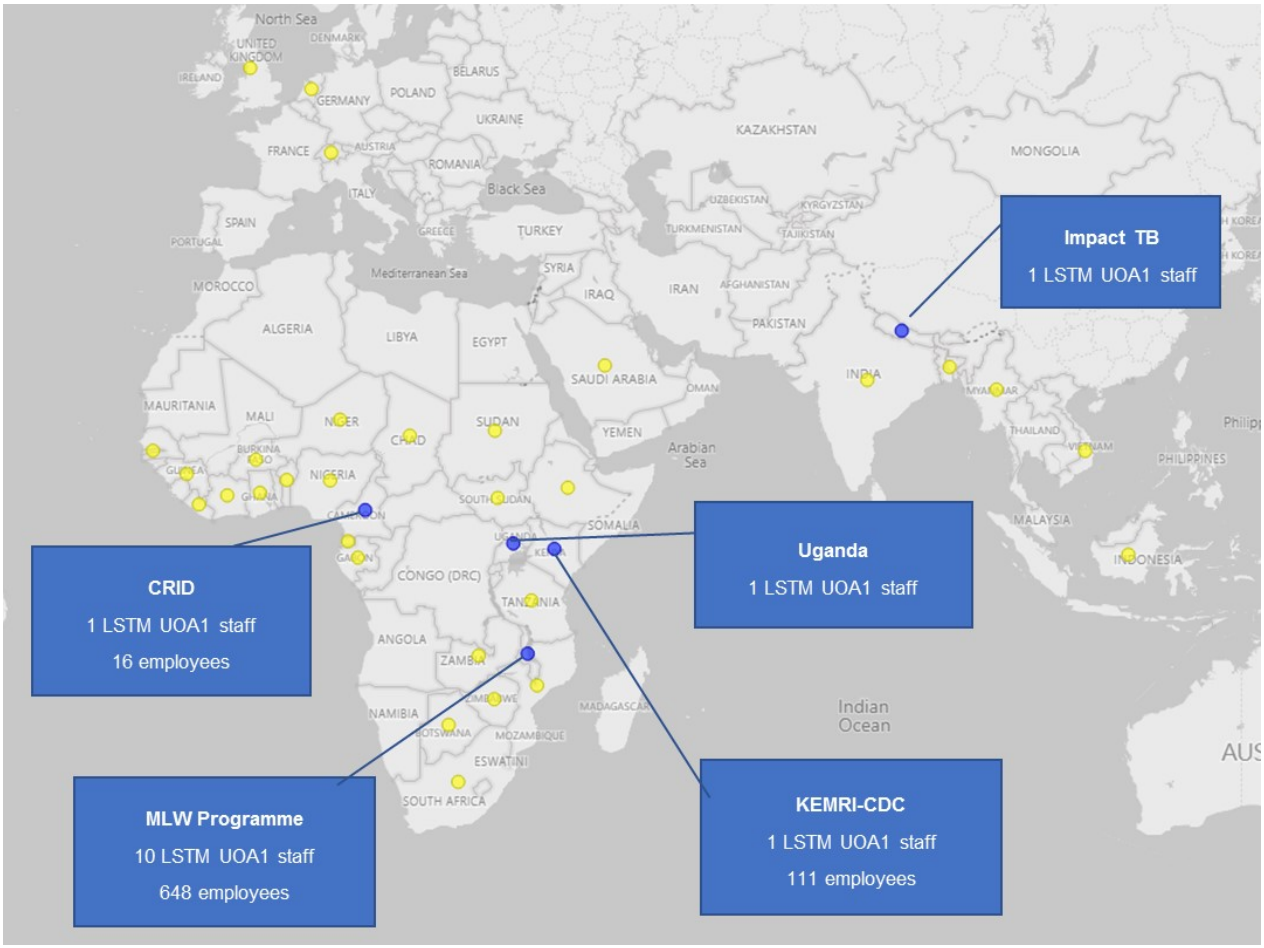


**Figure 3. Long term collaborations with resident UOA1 LSTM staff – blue symbols. International collaborators in LSTM UOA1 awards >£1M – yellow symbols.**

The work of UOA1 often requires long-term presence in LMICs, e.g. for field work on vectors or the clinical-laboratory study of human diseases. We offer the following major long-standing research facilities as examples of this UOA1 presence.

**The Malawi-Liverpool-Wellcome Programme**. LSTM holds the Wellcome Trust core grant for MLW (£25M) which now employs 648 staff. MLW was established by Molyneux (of LSTM) in 1995 with a mission to conduct excellent research and train the next generation of researchers (particularly Malawians). Now directed by Gordon (of LSTM), MLW is a constituent of the University of Malawi College of Medicine and a partner of both LSTM and UoL. The affiliation of LSTM staff in MLW is to Departments of CS, VB and IPH. MLW works on bacterial drug resistance (Feasey, Iroh Tam), viral immunology (Jambo), vector biology (Jones), mucosal immunology (Mwandumba), lung health (Rylance), sepsis (Morton), malaria epidemiology (Terlouw), community health (MacPherson) and health-behaviour (submitted to UOA2). LSTM awards in MLW total £58M since January 2014. MLW is based in the QECH Blantyre. In the present Census Period, LSTM has invested the following sums in MLW buildings. The *Learning & Teaching Centre* (2013; £2M) – as well as space for meetings this houses offices (thus freeing space in the *Malcolm Molyneux Research Laboratories* (1999; refurbished 2014 £0.6M). The negative-pressure ventilated laboratories (2015; £50k) have enabled research on pathogens such as TB. The *Adult Accident & Emergency Building* of QECH (2013; £1.3M) – standards of care have risen and high-quality clinical research can now be done. The *Clinical Research And Training Open Resource (CREATOR)* Building (4,324m$^2$; under construction and due to open 2023; £8.9M in partnership with UoL) - the first specialist postgraduate medical training centre in

Malawi, CREATOR will provide the most sophisticated (and open-resource) research environment in the country.

**The LSTM collaboration with KEMRI/CDC in western Kenya.** The *Kenya Medical Research Institute* (KEMRI) and US *Centers for Disease Control and Prevention* (CDC) has its campus at Kisian, close to Kisumu City. The campus is a registered NIH clinical research trial site and has world class certified laboratory facilities. The health and demographic surveillance system covers a population of ~250,000, providing a platform for population-based studies. ter Kuile leads the LSTM team, which is working on malaria, HIV, rapid diagnostic tests, paediatric gut health, mortality ascertainment, adolescent and women's health, sexual and reproductive health and female genital schistosomiasis. Other LSTM staff are submitted to UOA2. 111 staff are employed on LSTM projects.

**The LSTM collaboration with the Centre for Research in Infectious Diseases (CRID), Cameroon**. This collaboration was established in 2017 through a Wellcome Trust senior fellowship in biomedical sciences to Wondji who is also Executive Director of CRID. The collaboration has led to the award of several Wellcome fellowships through LSTM. The LSTM-CRID partnership also supports the £6.4M GCRF project PIIVEC (see above). A recent £2.2M renewal of Wondji's Wellcome senior fellowship further strengthens this collaboration with members of his group based between Liverpool and Yaoundé. Research activities at CRID focus on various topics of vector control including on malaria, arbovirus diseases and sleeping sickness using genetics, genomics and ecological approaches. A primary topic is the elucidation of molecular basis of insecticide resistance in malaria vectors and the assessment of its impact on the effectiveness of insecticide-based interventions. Through a collaboration with IVCC, CRID is also contributing to the validation of novel insecticides through lab and semi-field testing in Cameroon. 16 staff are employed on LSTM projects.

**The IMPACT TB research programme in Nepal** is led by Caws within the *Birat Nepal Medical Trust* (BNMT). Established in 2017 with Horizon 2020 funding (€5M). The core of the work is evidence generation to inform policy for LMIC TB interventions. The programme is also studying (a) mathematical models to inform interventions for TB, (b) molecular epidemiology of TB transmission, (c) socioeconomic support models and (d) the long-term impact of COVID-19 on access to TB care. Funders include the Nick Simons Foundation, Wellcome Trust, MRC and Australian National Health.

**Uganda**. LSTM includes several collaborations in Uganda that address research questions related to life-threatening infections, acute care and addressing knowledge gaps along the health system continuum, including understanding how and when individuals with severe infections and other severe illnesses seek hospital-based care and what factors influence their outcomes after being discharged from hospital severe infections. This work is led by Jacob who has been living and working in Uganda for 15 years. Key among LSTM's partnerships under Jacob are WALIMU (Kampala), a Non-Governmental Organization co-founded by Jacob in 2012 and implementing partner for ARCS (NIHR-funded), and Makerere University's Infectious Diseases Institute (Kampala), implementing partner for DRUM (MRC-funded), both described above. LSTM grants currently relevant to these partnerships total over £5.8M.

**Wider contributions**

***Public engagement (PE) activities:***
LSTM is committed to support for PE both locally and overseas and supports staff and postgraduate students to undergo training in PE. Locally, the COVID-19 pandemic has led to new on-line relationships such as engagement with primary schools within the Everton FC *Schools Supporters' Club* Programme. In addition, LSTM staff have been frequent presenters on the local radio 'Science Show', providing reassurance and information on the pandemic. Each LSTM international 'unit' runs PE with their own communities. For example, work in 2019 in Malawi included a PE focus around anti-microbial drug resistance involving the Health Ministry; this work won an award from the Wellcome Trust (£248,385) in October 2020.

***Indicators of wider influence include:***
Advisory group for the Chief Medical Officer on Prophylaxis for COVID-19 (Lalloo); Academy of Medical Sciences Overseas Development Assistance (ODA) committee (Hemingway); Commonwealth Association of Paediatric Gastroenterology and Nutrition (Allen);Gates Foundation (Hemingway, Taylor, Turner, Ward); German Centre for Infection Research; DZIF (Ward); Scientific Advisory Group for Emergencies UK Government (SAGE) for Ebola, Zika and COVID-19 (Lalloo); Medicines for Malaria Venture (Ward); NIHR COVID-19 Vaccine Research Delivery Group (Ferreira and Collins); NIHR Global Health Research (Lalloo); Public Health England Advisory Committee on Malaria Prevention in Travellers (Lalloo, Ranson); Wellcome Trust Surveillance and Epidemiology of Drug-resistant Infections Consortium (Feasey); Wellcome Trust Snakebite Priority Area International Scientific Advisory Board (Mwandumba); MRC Global Health Group (Lalloo)

47% of LSTM staff have sat on WHO advisory boards during the REF period including: WHO Technical Working Groups and Panels (Drug Resistance and Containment: Hastings; HIV self-testing: MacPherson; Insecticide resistance: Donnelly, Ranson; Schistosomiasis: Stothard; Sepsis: Jacob; Snakebite: Harrison, Lalloo; Vector Control Advisory Group: Ranson; Vector Control Pre-Qualification: Wondji; Zika: McCall).

***Honours and awards in the REF period include:***
African Research Leader (Jambo, Mwandumba)
Fellowship of the Royal Society; Sir Patrick Manson Medal Royal Society Tropical Medicine and Hygiene (Hemingway)
International Fellow of the American Society of Tropical Medicine and Hygiene (ter Kuile)
Royal Society Wolfson Fellowships (Jaffar, Ranson, Donnelly, Hughes)
Harvard - Chan School of Public Health Award (Jacob)
Honorary Member of The International Union Against TB & Lung Disease (Squire)
Royal Society Africa Prize (Mwandumba)
President British Society Parasitology (Taylor)

***Membership of major funding committees**:*
Wellcome Trust (Adams, Craig, Gordon, Jacob, Lalloo, Mwandumba, Ranson, Taylor); MRC (Allen, Biagini, Caws, Cuevas, Donnelly, Feasey, McCall, Mortimer, Gordon, Jaffar, Ranson); Irish Research Council (Urban); Newton Fund (Biagini, Hemingway); NIAID/NIH (Hastings, Hughes, McCall); NIHR (Rylance, Lalloo); Research Council Norway (Stothard); Royal Society (Hemingway, Pleass, Ranson, Taylor, Wondji); UKRI FLF ( Lalloo, Ranson); European Union (Biagini); EDCTP (Craig).

***Editors/associate editors/section editors of major journals**:*
Anaesthesia (Morton) Experimental Parasitology (Acosta-Serrano), Insect Molecular Biology (Paine), Medical and Veterinary Entomology (Reimer) Mobile Genetic Elements (Roberts), Parasites and Vectors (Weetman), PLOS Neglected Tropical Diseases (Acosta-Serrano, Feasey, Harrison, Lalloo), Parasitology (Stothard), Proceedings of the National Academy of Sciences (Hemingway); J Infection (Lalloo), Frontiers in Tropical Diseases (Taylor).

In addition to the above senior editorial roles, UOA1 staff are also members of editorial boards of a further 27 international journals.